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BOSTON UNIVERSITY

GRADUATE SCHOOL

Thesis

THE EFFECT OF THE ADRENAL SECRETIONS
ON
BLOOD SUGAR METABOLISM.

Submitted by

Solomon J. Gootman

(A. B., Boston University, 1932)

In partial fulfillment of requirements
for the degree of Master of Arts
1933

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THE EFFECT OF THE ADRENAL SECRETIONS ON BLOOD SUGAR
METABOLISM.

INDEX

Introduction.....	Page 1
Consequences of adrenalectomy.....	3
Importance of the medulla.....	4
Anatomy.....	5
Embryology.....	6
Cortex.....	6
Medulla.....	6
Accessory adrenal tissue.....	7
Comparative anatomy.....	7
Blood supply.....	8
Nerve supply.....	9
Color reactions.....	10
Adrenalin.....	11
Precursor of adrenalin.....	12
Adrenalin content of the glands.....	13
Absorption of carbohydrates.....	14
Conversion to glycogen and reversal.....	14
Relation of the liver to sugar metabolism....	16
Renal threshold for sugar.....	16
Role of the pancreas.....	17
Influence of adrenalin on sugar metabolism.....	18
Blood sugar level.....	22

THE JOURNAL OF THE ROYAL ANTHROPOLOGICAL INSTITUTE

1901

1	THE JOURNAL OF THE
2	ROYAL ANTHROPOLOGICAL INSTITUTE
3	1901
4	CONTENTS
5	THE JOURNAL OF THE
6	ROYAL ANTHROPOLOGICAL INSTITUTE
7	1901
8	CONTENTS
9	THE JOURNAL OF THE
10	ROYAL ANTHROPOLOGICAL INSTITUTE
11	1901
12	CONTENTS
13	THE JOURNAL OF THE
14	ROYAL ANTHROPOLOGICAL INSTITUTE
15	1901
16	CONTENTS
17	THE JOURNAL OF THE
18	ROYAL ANTHROPOLOGICAL INSTITUTE
19	1901
20	CONTENTS
21	THE JOURNAL OF THE
22	ROYAL ANTHROPOLOGICAL INSTITUTE
23	1901
24	CONTENTS
25	THE JOURNAL OF THE
26	ROYAL ANTHROPOLOGICAL INSTITUTE
27	1901
28	CONTENTS
29	THE JOURNAL OF THE
30	ROYAL ANTHROPOLOGICAL INSTITUTE
31	1901
32	CONTENTS
33	THE JOURNAL OF THE
34	ROYAL ANTHROPOLOGICAL INSTITUTE
35	1901
36	CONTENTS
37	THE JOURNAL OF THE
38	ROYAL ANTHROPOLOGICAL INSTITUTE
39	1901
40	CONTENTS
41	THE JOURNAL OF THE
42	ROYAL ANTHROPOLOGICAL INSTITUTE
43	1901
44	CONTENTS
45	THE JOURNAL OF THE
46	ROYAL ANTHROPOLOGICAL INSTITUTE
47	1901
48	CONTENTS
49	THE JOURNAL OF THE
50	ROYAL ANTHROPOLOGICAL INSTITUTE
51	1901
52	CONTENTS
53	THE JOURNAL OF THE
54	ROYAL ANTHROPOLOGICAL INSTITUTE
55	1901
56	CONTENTS
57	THE JOURNAL OF THE
58	ROYAL ANTHROPOLOGICAL INSTITUTE
59	1901
60	CONTENTS
61	THE JOURNAL OF THE
62	ROYAL ANTHROPOLOGICAL INSTITUTE
63	1901
64	CONTENTS
65	THE JOURNAL OF THE
66	ROYAL ANTHROPOLOGICAL INSTITUTE
67	1901
68	CONTENTS
69	THE JOURNAL OF THE
70	ROYAL ANTHROPOLOGICAL INSTITUTE
71	1901
72	CONTENTS
73	THE JOURNAL OF THE
74	ROYAL ANTHROPOLOGICAL INSTITUTE
75	1901
76	CONTENTS
77	THE JOURNAL OF THE
78	ROYAL ANTHROPOLOGICAL INSTITUTE
79	1901
80	CONTENTS
81	THE JOURNAL OF THE
82	ROYAL ANTHROPOLOGICAL INSTITUTE
83	1901
84	CONTENTS
85	THE JOURNAL OF THE
86	ROYAL ANTHROPOLOGICAL INSTITUTE
87	1901
88	CONTENTS
89	THE JOURNAL OF THE
90	ROYAL ANTHROPOLOGICAL INSTITUTE
91	1901
92	CONTENTS
93	THE JOURNAL OF THE
94	ROYAL ANTHROPOLOGICAL INSTITUTE
95	1901
96	CONTENTS
97	THE JOURNAL OF THE
98	ROYAL ANTHROPOLOGICAL INSTITUTE
99	1901
100	CONTENTS

Relative importance of the cortex to life.....	Page 26
Intoxication theory.....	26
Cortex and blood sugar	26
Table 1	
Cortical extracts	28
Table 2	
Summary	33
Bibliography	35

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COMMISSION

ON THE PROGRESS OF THE WORK DURING THE YEAR 1900

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AT THE ANNUAL MEETING, 1901

INTRODUCTION

Metabolism in general, as well as in many of its details, is governed by the activity of endocrine glands, or glands of internal secretion. In the human body there are approximately six of these glands which are known to secrete directly into the blood very minute amounts of active substances. These active secretions are variously called chemical messengers, hormones, or autacoids. The best known glands of internal secretion are the adrenals, thyroids, pancreas, parathyroids, pituitary, and gonads (ovaries or testes. Each of these glands secretes into the blood one or more substances which influence the activity of some organ or organs. The chemical messengers derived from the endocrine glands may bring about extraordinary shifts in the course or rate of normal metabolism.

The mechanism of the internal secretions is complex in its mode of action. It is believed that the active substances are discharged directly into the blood through the capillary blood vessels with which the glands are well supplied, and that they pass with the circulating blood to other organs and tissues, and stimulate them to activity or bring about other characteristic changes. Their activities are often synergic and in some cases there is good reason to believe that an antagonism exists between different glands. The physiology of many of these glands is more or less intimately connected with carbohydrate

metabolism. This is particularly true in the case of the pancreas and adrenals.

Various experiments show that the adrenal secretions increase the metabolic rate. Extirpation of these glands may, therefore, lead to a lowered metabolism. The most striking effects of the internal secretions in modifying metabolism are to be noted in abnormalities which develop in diseased conditions. (58)*

In the sixteenth century the adrenal glands were observed, for the first time, by Eustachius who called them glandulae renibus incumbentes. For a long time afterwards the adrenal glands were considered of slight account and were the subject merely of anatomical study and of curious speculations. Riolanus in 1628 called them glandulae suprarenales. (7)

It is interesting to note that our earliest knowledge of the internal secretions was obtained not by purely laboratory experiments but through the observation of pathological cases. In 1849, Addison (2) observed that after a certain kind of anemia, a peculiar and fatal disease often associated with bronzing of the skin, the autopsy constantly showed lesions of the adrenal capsules. This condition now known as Addison's disease, though often associated with

*(58) pp. 353-355

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part of the year 1882.

The first part of the year 1881 was marked

by a series of severe frosts, which were

followed by a period of moderate weather.

The second part of the year 1882 was

marked by a series of severe frosts, which were

followed by a period of moderate weather.

The first part of the year 1883 was marked

by a series of severe frosts, which were

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1884. The first part of the year 1884 was

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followed by a period of moderate weather.

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The first part of the year 1885 was marked

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The second part of the year 1885 was

marked by a series of severe frosts, which were

tuberculosis of the adrenal glands as in the cases studied by Addison, may be due to the destruction of these glands by any process.* Addison's disease is believed to be due to hypofunction of the adrenals, and it is probable that the more severe symptoms are the result of the destruction of the adrenal cortex.

In 1856 Brown-Séquard, (12) stimulated by the work of Addison, undertook extirpation experiments to ascertain the function of the adrenals, and announced that these glands were indispensable to life, because all of his animals including rabbits and rats, died within a few days after bilateral adrenalectomy.

CONSEQUENCES OF ADRENALECTOMY

Extirpation of the adrenal glands is usually fatal; but the time element differs in various animals. If the whole glands are removed death results. Dogs and cats rarely live more than 48 hours, if both glands are extirpated in one operation; but they may live from six to ten days if the second gland is removed several weeks after the first. Elliott (23) reported that of twenty-one cats in which both glands were excised in one operation over ninety per cent died in from 18 to 48 hours. Stewart and

*The more important symptoms are pigmentation or bronzing of the skin, excessive muscular weakness leading to prostration, mental depression and other nervous symptoms, gastrointestinal disturbance including vomiting, atrophy of the sex organs, and hypoglycemia.

Rogoff (50) removed the adrenals from 29 dogs in two operations, and found that 90 per cent died between the fourth and sixteenth days.

Gaunt (25) studied the survival of 185 bilateral adrenalectomized rats from five different colonies, and reported that the mortality among laboratory bred rats was 95 per cent within 20.5 days with an average life-span of seven days. Animals from the fifth colony (of unknown pedigree) showed a 50 per cent survival for thirty days after adrenalectomy.

In man quick death follows lesions in the glands. (40)*

Experiments show that the loss of one adrenal is not fatal. In fact, Kuriyama (35) has even observed that the remaining gland often hypertrophies, and is able to keep the animal in a normal condition.

IMPORTANCE OF THE MEDULLA

Experimental evidence indicates that the medullary tissue is not indispensable to life and health. In some animals it is very difficult to remove by operation all chromophil tissues; but this tissue is present mostly in the medulla of the adrenal gland and the bulk of the medulla can be removed without producing death in experimental animals.

In a personal communication Dr. Wyman stated that complete removal of the medullary tissue may be tolerated

*(40) pp. 691-694

in rats by transplantation of the glands. Both adrenals are transplanted in the abdominal muscles. Autopsy of animals in which the transplants are successful shows that the cortical tissue has regenerated while the medullary tissue has disappeared. The effects equivalent to extirpation or lack of medullary tissue may thus be investigated because rats have no accessory chromophil tissue.

ANATOMY

Like most endocrine organs, the adrenals are subject to great variation. In man, the adrenals are two small, highly vascular organs, usually situated at the upper poles of the kidneys and both weigh together about 8 or 9 grams. Of the two, the left is usually the larger. (31) Each adrenal gland is composed of an external portion or cortex, and a central portion or medulla. The boundary between the layers of the cortex and medulla is not sharply delimited.* The cortex and medulla, however, have very little in common except their anatomical position. The differences in histological structure, in embryological development, and in comparative anatomy, indicate that these two portions of the gland serve quite distinct functions in the body. (39) **

*My observations made in experiments with rats show that the differentiation between the medulla and cortex is so marked that it can be clearly seen by the naked eye.

** (39) pp. 130-131

EMBRYOLOGY

The adrenal glands are developed from two distinct sources.

Origin of the cortex.

The cortex is derived embryologically from the epithelial cells of the mesoderm lining the body cavity. The cells of the cortex are arranged in three concentric zones or layers. The comparatively large adrenals which are found in the human fetus are due in considerable measure, to the remarkable development of the fetal cortex. The fetal cortex, although it forms the bulk of the gland at birth, undergoes a process of progressive degeneration during the last ten weeks of embryonic life. In post-natal life the inner and middle layers of the cortex degenerate. The size of the adult cortex depends on the regenerative ability of the outer cells which continue to multiply throughout life. (31)

Origin of the medulla

The medulla arises from the same embryonic structures as the sympathetic nervous system. Lutz and Case (36) have found indications of the presence of adrenalin in the gland of the chick as early as the eighth day of incubation. Positive chromaffine reactions in the mouse-adrenal were obtained by Miller (41) approximately fourteen to fifteen days after fertilization.

My dear Mr. [Name]

Received of you

the sum of [Amount] for [Purpose] and I have
the pleasure to acknowledge the receipt of the same.
The sum of [Amount] is hereby acknowledged as
received of you for [Purpose] and I have the
pleasure to acknowledge the receipt of the same.
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received of you for [Purpose] and I have the
pleasure to acknowledge the receipt of the same.

I am, Sir, very respectfully,
Your obedient servant,

[Signature]

[Name]

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The sum of [Amount] is hereby acknowledged as
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pleasure to acknowledge the receipt of the same.

I am, Sir, very respectfully,
Your obedient servant,

[Signature]

[Name]

Accessory adrenal tissues

Accessory adrenal tissue is located in various places in mammals. Common situations for accessory cortical tissue are the retroperitoneum, the surface of the liver, the kidneys, the space between the testis and epididymis in the male, and the vicinity of the broad ligament in the female. Accessory chromophil tissue may be found in the sympathetic ganglia, in the carotid body, and in front of the abdominal aorta.(57)*

COMPARATIVE ANATOMY

The adrenals are found in all classes of vertebrates and in most of these classes chromophil tissue is also found outside the glands. In the lower vertebrates the cortex and medulla are entirely distinct organs. This can be seen in the Elasmobranchs where the cortical organ is separate from the medullary. The cortical tissue is here found between the kidneys and termed the "interrenal body". The chromophil tissue is a series of paired bodies derived from the sympathetic ganglia and arranged along the sympathetic nerves. Lutz and Wyman (37) found that the interrenal bodies corresponding to the homologues of the cortical tissue of the higher vertebrates gave negative tests for adrenalin while the chromophil bodies always gave positive tests. They concluded that the cortical tissue of the adrenal glands of higher vertebrates is not involved in the production of adrenalin. In the higher

*(57) p.146

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Vol. 100, Part 1, 1970

CONTENTS

1. The Prehistory of the British Isles, by J. G. Hurst

2. The Prehistory of the British Isles, by J. G. Hurst

3. The Prehistory of the British Isles, by J. G. Hurst

4. The Prehistory of the British Isles, by J. G. Hurst

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18. The Prehistory of the British Isles, by J. G. Hurst

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20. The Prehistory of the British Isles, by J. G. Hurst

species the cortex and medulla become closely associated. In amphibians, in which the mesonephros persists, the adrenals are sometimes represented by small masses of tissue just above the kidneys. There is a partial connection between the medullary and cortical tissues. In reptiles and birds the two tissues become concentrated and may be found in definite locations. In mammals, these glands are well developed. The chromaphil tissue penetrates into the interrenal and is enclosed by it, forming the medulla of the definite adrenal gland. But, even in mammals in addition to the adrenals small accessory masses of chromaphil and cortical tissues are found in other regions. (40)* (57)**

BLOOD SUPPLY

In humans, blood is freely and plentifully supplied to the adrenals by the suprarenal, inferior phrenic, and renal arteries. These arteries enter the capsule of the gland and there give off many branches which supply a rich network of blood spaces in the cortex. The amount of blood passing through the glands is very large compared to their size, being about 5 - 6 cc. per gram of gland per minute in dogs and cats. Neuman (43) showed that the adrenals are probably the most highly vascularized glands in the body and that the normal blood flow

* (40) p. 690

** (57) pp 139 - 153

in the cat may reach 7 cc. per gram of gland per minute. In the higher mammalian types the greater part of the blood supplied to the gland comes first, however, into intimate relation with cortical elements. Henderson (30) has called attention to a rich network of blood spaces between the columns of cells in the cortex through which blood passes inward to very large sinuses in the medulla. Small venous channels collect the blood and discharge it into the various branches of the central vein. The lumbo-adrenal vein which emerges at the hilus empties the blood either into the vein from the kidney or directly into the large abdominal vein, the inferior vena cava.

NERVE SUPPLY

The sources of the glandular nerve supply in man are not completely known, but it is well established that the chief innervation is directly from the splanchnics. The cortical tissues are sparsely supplied with nerves and may function when entirely deprived of a nervous supply.

The medullary tissues, however, are richly supplied with nerves which entirely control the function of the medulla. (31) The secretion of the medulla of the adrenal gland is believed to reinforce the activity of the sympathetic nervous system during conditions of stress. The adrenal medulla and the sympathetic nervous system are

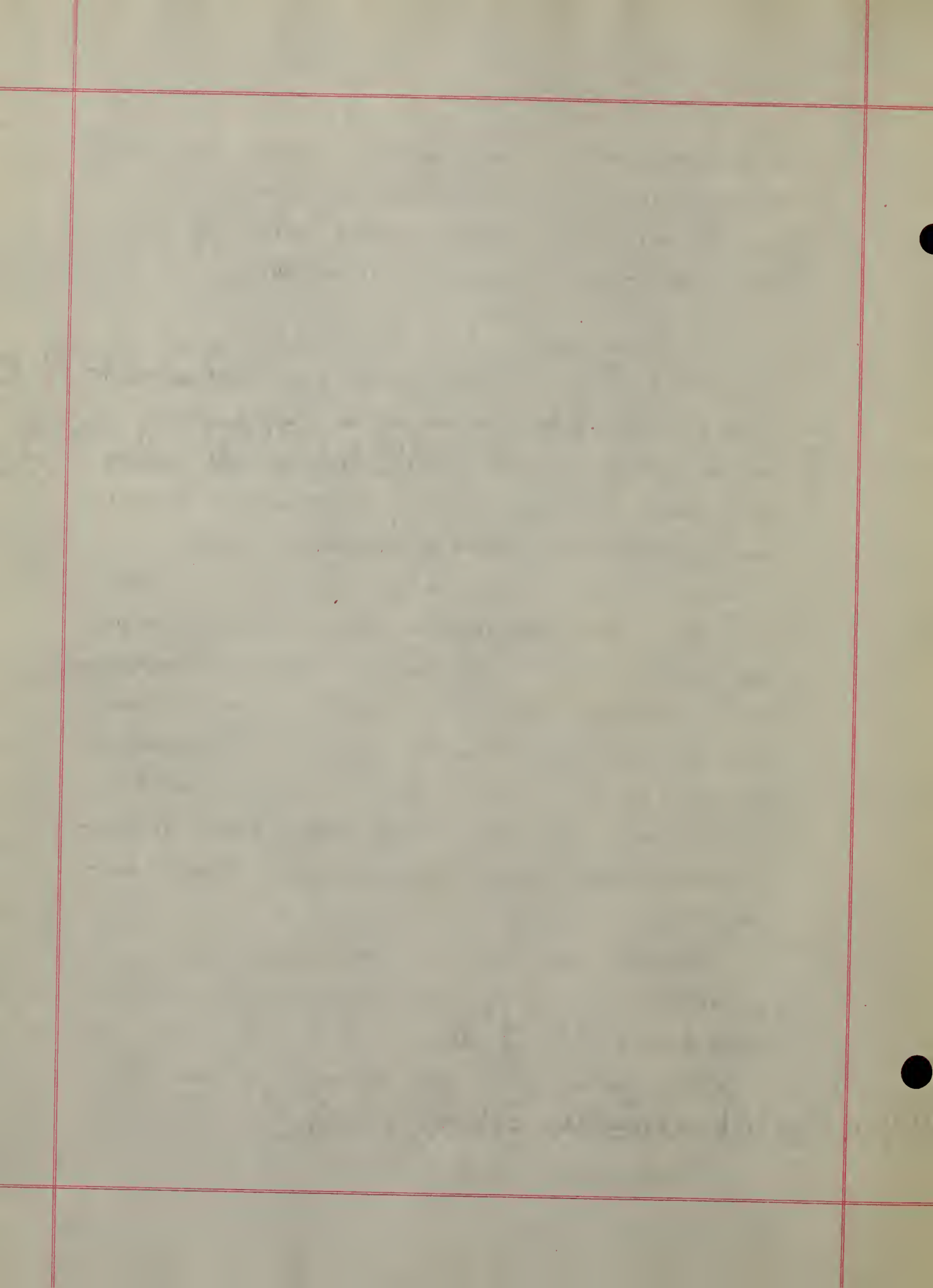
closely related both functionally and anatomically. The connector fibers of the splanchnic nerve can be traced into the medulla to end round ganglion cells, and also round the chromaphil cells themselves. (59)*

COLOR REACTIONS

The two tissues of the adrenal gland give different color reactions. An exposed cortical portion has a yellowish color, but the cortical cells are not stained by potassium dichromate ($K_2Cr_2O_7$). The medulla is partly stained reddish brown after treatment with potassium dichromate. This peculiar brown stain is taken by some other cells also, and tissue so stained is called chromaphil tissue. The staining power appears to be dependent upon or correlated with the presence of the active principle of the medulla, since the amount of the hormone and the depth of stain rise and fall together. The active principle obtained in extracts of adrenal glands is quantitatively proportional to the amount of chromaphil substance.

Adrenalin, the extract of the medullary tissue, in extraordinarily minute amounts usually affects the structures innervated by the sympathetic division of the autonomic nervous system precisely as if they were receiving the nervous impulses.

*(59) p.131



ADRENALIN

The medullary portion of the adrenal glands has a particular relation to the activity of the sympathetic nervous system. Oliver and Schafer (44) reported in 1895 that the outstanding results of an intravenous injection of an extract of the adrenals in cats and other mammals, were:

- (1) augmentation in blood pressure
- (2) stimulation of the heart
- (3) vasoconstriction in the splanchnic organs
- (4) the effects of the extract only lasted for a short time.

The effects produced are almost all such as are produced by stimulating the sympathetic nerves, hence the substance is said to be sympatho mimetic. Further research by different investigators showed that the substance that produced these actions was present in the medulla, and not in the cortex.

The isolation of an active principle from the adrenal medulla in an impure condition was first accomplished in this country in 1897 by Abel and Crawford (1). They obtained a monobenzoyl product and called it epinephrin. Four years later, Takamine (55) isolated the active principle from the adrenal gland in a crystalline condition. Aldrich (3) independently prepared this substance by a different method and assigned to it the empirical

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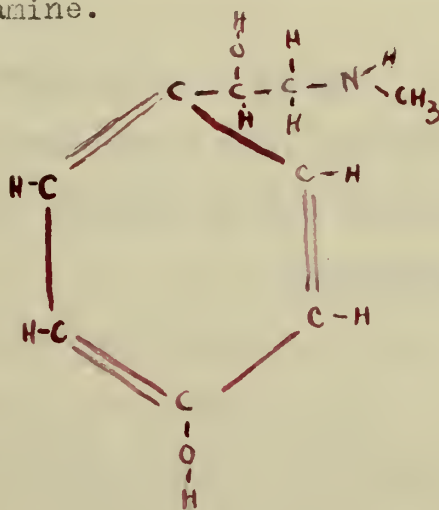
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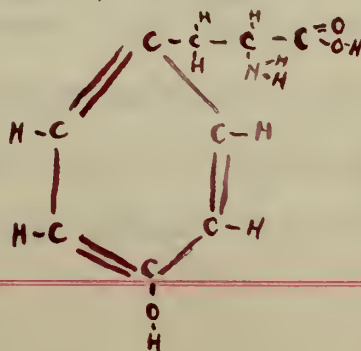
formula of $C_9H_{13}O_3N$. Jowett (32) analyzed carefully purified material and confirmed the formula proposed by Aldrich. Finally, the racemic mixture was synthesized by Stolz (52) in 1907, and later the levo-rotatory form was also synthesized.

Adrenalin has been indentified as L-3, 4-dihydroxy-phenylethanolmethylaniline.



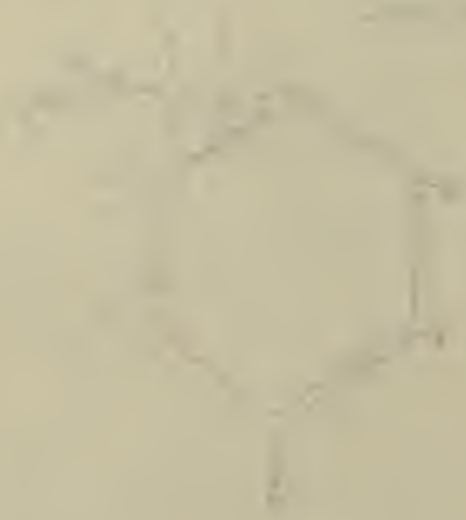
Precursor of adrenalin

While nothing is known concerning the precursor of adrenalin in the body, the fact that adrenalin is an hydroxylated aromatic derivative has favored the belief that it is synthesized by the gland, in vivo, from tyrosine. Adrenalin possesses a structure suggesting a relationship to tyrosine (α -amino - p - hydroxy phenylpropionic acid.)



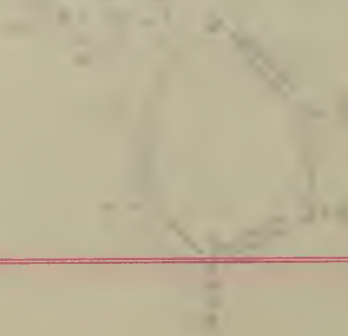
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Tyrosine was one of the first amino acids to be obtained from a protein. It may be prepared from casein. In fact, one investigator reported increases in the adrenalin content of the glands when they were incubated with tyrosine; but this observation could not be confirmed by others. (42)*

Adrenalin content of the glands.

Folin, Cannon, and Denis (24) determined the amount of adrenalin normally present in the adrenals of:

	<u>Adrenalin per gm. of gland.</u>
sheep.....	2.96 mgs
cats.....	1.36 "
cattle.....	3.96 "
rabbits.....	3.22 "
dogs and monkeys.....	2.20 "
human adults suddenly killed.....	1.00 "

Stewart (47) claimed that the amount of adrenalin in arterial blood cannot be greater than $1:2 \times 10^8$ to $1:1 \times 10^9$. The output in cats he found to be constant on an average of about 0.00025 mgs. per kgm. of body weight per minute, and the same in dogs. Cannon and his co-workers (14) who, particularly have studied adrenalin physiology estimate that much larger quantities of adrenalin are present in the adrenals, and claim that adrenalin is liberated only in

* (42) p. 413

1. The first part of the report is a general introduction to the subject of the study. It discusses the importance of the problem and the objectives of the research. It also mentions the scope of the study and the methods used.

2. The second part of the report is a detailed description of the experimental work. It includes a description of the apparatus used, the procedure followed, and the results obtained. It also discusses the errors and limitations of the experiment.

3. The third part of the report is a discussion of the results. It compares the results with the theoretical predictions and with the results of other experiments. It also discusses the implications of the results and the conclusions drawn from the study.

4. The fourth part of the report is a conclusion. It summarizes the main findings of the study and states the conclusions drawn from the results. It also mentions the suggestions for further work and the acknowledgments.

emotional states.

ABSORPTION OF CARBOHYDRATES

The most important carbohydrate materials absorbed are the simple sugars glucose, fructose, and galactose. Polysaccharides are usually digested into simple sugars by the enzymes of the pancreas and intestine before absorption. Disaccharides may be hydrolyzed in the mucosa to glucose during their passage through the intestinal walls. The final products of carbohydrate digestion are absorbed into the blood in the form of glucose. (40)* Cori and Cori (18) reported that rats suffering from adrenal insufficiency absorb sugar slower than normal rats.

Conversion to glycogen and reversal

After glucose is absorbed, it is carried to the liver by the portal vein. If there is an immediate need for energy, the sugar passes through the liver and enters the general circulation. It diffuses from the blood into the tissues and is completely oxidized to carbon dioxide and water thus liberating a maximum of energy. If there is not an immediate need for energy, the liver cells remove the excess glucose and synthesize it into glycogen, in which form it is stored. The absorption of carbohydrates causes a rise in the blood sugar concentration, but the

* (40) p. 468

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increased amount of sugar in the blood accounts for a very small fraction of that which is absorbed. The amount of glycogen in the liver increases very greatly under such conditions, and it is estimated that as much as a half-pound of glycogen can be stored in the liver of an adult. The total glycogen content of the muscles may be roughly the same as the total content of the liver.

During periods when no absorption is taking place, the tissues of the body derive energy from the glycogen which is split again into glucose and carried by the blood to the tissues. The process of formation of glycogen is called glycogenesis, and occurs most rapidly during the absorption, when the concentration of glucose in the blood is high. The reverse process called glycogenolysis takes place especially when absorption is not taking place. Evidence indicates that it is the liver glycogen (at least in the main) which undergoes hydrolysis to produce blood sugar. (58)* Presumably, both the formation and the hydrolysis of glycogen takes place under the influence of the same enzyme (glycogenase).

Normally the concentration of glucose in the blood determines to a large extent whether glycogenesis or glycogenolysis will predominate, though there are other mechanisms which control the process. (15)**

*(58) pp. 381-383

** (15) pp. 273-276

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Relation of the liver to sugar metabolism.

Glycogen is normally present in the liver of well fed animals. The most important known function of the liver is to regulate the concentration of sugar in the blood. If the blood sugar becomes insufficient, liver glycogen is mobilized by impulses from the sympathetic nerves. The store of liver glycogen is utilized in the form of sugar, the fuel for the maintenance of energy processes.

Mann and Magath (38) (39) showed that in hepatectomy there is a progressive decrease of the blood sugar level. Further experiments have demonstrated that the liver must be regarded as the source of glucose in the blood, and that the muscles play little or no part in maintaining the normal level of blood sugar. Extraordinary shifts in carbohydrate balance in the organism may be brought about, however, by the secretions of the adrenals and pancreas.

Renal threshold for sugar.

In normal human subjects the glucose content of blood is about 100 mgs. in 100 cc. of blood, or 100 mgs. per cent. The variation of sugar in the blood may be from 80 mgs. to 160 mgs. per cent. The former represents the level attained on fasting for twenty-four hours, while the latter concentration may be reached after partaking of a meal rich in carbohydrates or sugar.

A rise in blood sugar above 160 mgs. per cent, causes

THE HISTORY OF THE CITY OF BOSTON

From the first settlement of the city in 1630 to the present time. The city of Boston was founded by a group of Puritan settlers who came to the Massachusetts Bay in 1630. They were led by John Winthrop, who gave the city its name. The city grew rapidly and became one of the most important cities in the New England colonies. It was the site of the Boston Tea Party in 1773, which led to the American Revolution. The city was also the site of the Battle of Boston in 1775, which was a decisive victory for the British. The city has since become a major center of commerce and industry in the United States.

THE CITY OF BOSTON

The city of Boston is located on the eastern shore of Massachusetts Bay. It is the largest city in the state and is one of the most important cities in the United States. The city is known for its rich history and its many cultural attractions. It is also known for its excellent education system and its many parks and recreational areas. The city is a major center of commerce and industry and is home to many of the largest corporations in the United States.

THE CITY OF BOSTON

The city of Boston is a major center of commerce and industry in the United States. It is home to many of the largest corporations in the country and is a major hub for international trade. The city is also a major center of education and research, with many of the world's leading universities and research institutions located there.

marked excretion through the urine. The kidneys ordinarily hold back the glucose until there is about 100 mgs. per cent of sugar, but when the sugar concentration has reached this value, it is said to have reached the renal threshold. The renal threshold varies slightly in different healthy individuals, * but in the light of many investigations the accepted figure is from 160 to 180 mgs. per cent.

If the concentration of sugar in the blood falls to 70 mgs. per cent or lower, weakness, fatigue, and hunger are manifested. Symptoms of incoordination, profuse sweating, pallor, and delirium are exhibited if the blood sugar concentration is further reduced. (15)**

ROLE OF THE PANCREAS.

The internal secretion of the pancreas (insulin) is important and indispensable to make the blood sugar available for utilization. Lesions in the pancreas are observed in cases of diabetes, and animal experiments show that removal of the pancreas brings on diabetes. A condition in which glucose is excreted rather than utilized is found in such cases. In the absence of insulin, the glucose concentration of the blood is maintained above the

* The chief value in determining the renal threshold for sugar is in connection with the diagnosis of renal glycosuria as contrasted with true diabetes.

** (15) pp. 98 - 103

kidney threshold and there is continuous glucose excretion or glycosuria.

When insulin is injected subcutaneously it produces definitely demonstrable chemical effects. The blood sugar concentration falls, depending on the dosage, to levels below normal. Some of the glycogen may disappear from the liver. If an overdose is taken, unconsciousness, convulsions, and even death may result. The effects of an overdose of insulin or hypoglycemia may be ameliorated by simultaneously eating or injecting glucose. (57)* In an excellent review, Cori (17) has emphasized that insulin and adrenalin may be factors of equal importance in regulating carbohydrate metabolism.

INFLUENCE OF ADRENALIN ON SUGAR METABOLISM.

A very important discovery made by Blum (5) was that the subcutaneous or intravenous injection of adrenalin greatly increased the blood sugar provided the liver contained glycogen, and therefore, produced hyperglycemia and glycosuria.

The adrenal glands were thus brought into relationship with glycogen conversion. Since that time much experimental work has been done in an attempt to determine the relative importance of adrenalin and the nervous system in regulating the level of blood sugar.

* (57) pp.66-69

The question that arises is whether the conversion of glycogen to glucose upon stimulating the splanchnics is due to the direct effect of the stimulus on the cells of the liver, or whether it is the indirect effect of stimulation of the adrenals, since these splanchnic nerves supply both organs. (40)*

To explain the significance of adrenalin Cannon (14) (15) has postulated the theory that this substance is secreted only during emotional stress of pain, hunger, fear, and rage, and enables the organism to cope with emergencies.

The increase of adrenalin and the increase of sugar in the blood are concomitantly reflex in character and because reflexes are generally useful responses, the secretion of adrenalin is beneficial. During emotional stress there is a mass shifting of the blood from the skin and viscera to the organs involved in neuromuscular exertion. The blood pressure is raised, the heart is steadied in rate, and made to beat more powerfully. The entire animal organism is toned up to maximum working capacity in the face of danger. As a result of these conditions, the body has to be maintained at a maximum energy level. Fear and rage, which accompany life and death struggles and flight, excite the secretion of adrenalin into the circulating blood

*(40) pp. 820-824

and reinforce the activity of the sympathetic. There is consequently a mobilization of an increased supply of ready fuel in the form of blood sugar. Emotions, therefore, stimulate the adrenals to liberate adrenalin and the prompt mobilization of sugar. It may be concluded that the adrenal glands are essential factors in emotional glycosuria.

The Harvard School of workers led by Cannon have accumulated much evidence in the last decade in support of the classical view of the effects of adrenalin in emergencies. The increased concentration of blood sugar has been attributed to the increase in the liberation of adrenalin into the blood stream which acts on the liver causing a breakdown of glycogen. Glycogen is called upon in times of need, changed and set free into the blood as sugar. In the absence of glycogen, adrenalin may even convert fats and proteins into glucose. It is believed, therefore, that the normal function of the adrenal medulla results in stimulating glycogenolysis.

In opposition to Cannon's emergency theory of adrenalin function Stewart and Rogoff (48) reported that the formation and storage of glycogen in the liver is not affected by the removal of both adrenals from rabbits. These authors also observed that extirpation of the adrenals in rats produced no essential changes in the capacity of the liver

The following is a list of the names of the persons who have been elected to the office of the President of the United States, from the year 1789 to the present time. The names are given in the order in which they were elected, and the year of their election is given in parentheses. The names are given in the order in which they were elected, and the year of their election is given in parentheses.

George Washington (1789)
John Adams (1797)
Thomas Jefferson (1801)
James Madison (1809)
James Monroe (1817)
John Quincy Adams (1825)
Andrew Jackson (1829)
Martin Van Buren (1837)
William Henry Harrison (1841)
Francis Pickens (1857)
Abraham Lincoln (1861)
Andrew Johnson (1865)
Ulysses S. Grant (1869)
Rutherford B. Hayes (1877)
James A. Garfield (1881)
Chester A. Arthur (1881)
Grover Cleveland (1885)
Benjamin Harrison (1889)
William McKinley (1897)
Theodore Roosevelt (1901)
William Howard Taft (1909)
Woodrow Wilson (1913)
Calvin Coolidge (1925)
Herbert Hoover (1929)
Franklin D. Roosevelt (1933)
Dwight D. Eisenhower (1953)
John F. Kennedy (1961)
Lyndon B. Johnson (1963)
Richard M. Nixon (1969)
Jimmy Carter (1977)
Ronald Reagan (1981)
George H. W. Bush (1989)
Bill Clinton (1993)
George W. Bush (2001)
Barack Obama (2009)
Donald Trump (2017)

The following is a list of the names of the persons who have been elected to the office of the Vice President of the United States, from the year 1789 to the present time. The names are given in the order in which they were elected, and the year of their election is given in parentheses. The names are given in the order in which they were elected, and the year of their election is given in parentheses.

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to form and store glycogen.

Kuriyama (33) observed that the injection of adrenalin in fasting rabbits can cause an increase of the glycogen content of the liver. He also (34) made a number of determinations on rats, and found that adrenalectomized animals showed a significant disability to store glycogen when compared with normal animals.

Cori and Cori (19) reported that adrenalectomized rats and mice showed an almost complete disappearance of liver glycogen when fasted for twenty-four hours, although the muscle glycogen is scarcely affected beyond that of similarly starved normal animals. After the injection of adrenalin in rats the glycogen diminished in the body and increased in the liver. They believe that the decrease of muscle glycogen is due to its conversion into blood sugar, the excess of which is changed into liver glycogen. Hence, it is the muscle glycogen that, under the effect of adrenalin, produces the increased amount of blood sugar. They concluded, therefore, that the effect of adrenalin is more potent on the glycogen of the muscle than on the liver. Moreover Cori (17) has called attention to the fact that the injection of adrenalin does not inhibit the synthetic process of glycogenesis in the liver. He has found that liver glycogen does not entirely disappear even during prolonged starvation, but that the liver glycogen utilized is due to



the breakdown of protein, fat, and other substances into glucose. He states that until recently it was taught that adrenalin causes hyperglycemia because such an excess of sugar is formed in the liver that the capacity for sugar utilization in the tissues is exceeded.

BLOOD SUGAR LEVEL.

Cori (17) has pungently summarized the now generally accepted view that a rise in blood sugar elicits a secretion of insulin and that a fall in blood sugar below a certain level is followed by an automatic discharge of adrenalin. The mechanism of blood sugar regulation (production and utilization) is believed to be connected with the action of these two hormones.

According to Cannon (14) the body is able to control the blood sugar under abnormal conditions by bringing into action the combined efforts of the sympathetic and adrenal mechanisms. During the emotional conditions of pain, hunger, fear and rage the mobilization of sufficient blood sugar is due partly to impulses along the sympathetic nerves and partly to the additional effect of the secretion of adrenalin. It has been shown that the increased adrenal secretion is a more important factor in liberating sugar from the hepatic stores than the direct action of nerve impulses.

Cannon and de la Paz (16) were the first to show that secretion of adrenalin is stimulated during emotion. This was done by comparing the concentration of adrenalin in the blood of normal cats with the concentration observed when the cats were frightened by the barking of a dog. Cannon and his co-workers (14)* have particularly developed this phase of adrenalin effects. They have shown that nervous excitation of adrenalin secretion produces an un-failing hyperglycemia resulting in glycosuria. They have also observed a transient glycosuria in groups of students after severe examinations and at the close of important athletic contests.

The emergency theory of Dr. Cannon has been amply substantiated by the researches of many physiologists.

Elliott (22) showed that the secretion of adrenalin is controlled by the splanchnic nerves. During severe hypoglycemia there is a reflex discharge of adrenalin from the medulla; but when the adrenals are inactivated the effects are absent in spite of severe hypoglycemia.

Griffith (26) has demonstrated that strong stimulation of an afferent nerve raises the blood sugar, chiefly by activating the adrenal glands. Any center, therefore, that controls the amount of adrenalin discharged into the blood might be regarded as a center that influences carbohydrate mobilization.

* (14) pp. 49-79

Brooks (11) believes that the fact that reflex rises in blood sugar equal to those produced in animals with intact central nervous systems are obtained after extirpation of the fore-brain, mid-brain, and the anterior portion of the medulla oblongata does not indicate that the higher centers have no ability to control carbohydrate mobilization.

Edwards, Richards, and Dill (21) have observed that exercise with little or no emotional stress in normal men does not produce hyperglycemia; but when emotional factors are involved the blood sugar is increased, and glycosuria is evident.

Certain investigators failed to confirm the experimental evidence in favor of the emergency theory of adrenalin function.

Stewart and Rogoff (50) contended that there is no evidence that the rate at which glycogen is changed into blood sugar is influenced by the adrenalin output from the adrenals.

Stewart (47) stated that the best evidence for the view that the adrenalin output during emotion exerts no important function in glycogenolysis is that, after its suppression, the animals do not differ notably from normal animals in the blood sugar content or in a variety of other ways in which Cannon observed significant differences.

Experiments by Cori and Cori, (20) on the influence of adrenalin on blood sugar utilization, indicated that animals injected with adrenalin are unable to utilize glucose at the same rate as the normal uninjected animals. These experiments showed that animals supplied with adrenalin have a diminished necessity for blood sugar in the tissues.

Cori (17) has further stated that the injection of adrenalin in rats causes an accelerated disappearance of muscle glycogen and at the same time liver glycogen in the rat and rabbit is formed in excess over that mobilized, so that there is a rise in hepatic glycogen (instead of a glycogenolysis). He has found that the increase in liver glycogen, and in blood and tissue sugar may be accounted for by the disappearance of muscle glycogen under the influence of injected adrenalin.

Cannon (13) objected to experiments that tend to show continuous secretion of adrenalin because experimental evidence was obtained during disturbing conditions. He concludes that adrenalin is not secreted continuously, but only in emergencies.

It is evident from the above discussion of the medullary function that the emergency theory of adrenalin function is the accepted explanation for normal adrenalin activity in the organism. The emergency theory has now become a physiological fact.

RELATIVE IMPORTANCE OF THE CORTEX TO LIFE.

The cortex, in contrast to the medulla, is the indispensable portion of the adrenal. Death in adrenalectomized animals is due primarily to the absence of the cortical tissue. Knowledge of the functions of the adrenal cortex has been developing in recent years. Considerable evidence is available tending to show some relationship between the cortex and normal carbohydrate metabolism. Recently a hormone has been extracted from the cortex in a highly concentrated form. Animals from which all the adrenal tissue has been removed may be kept alive with these extracts.

INTOXICATION THEORY.

The terminal picture after adrenalectomy has all the symptoms of ^{an} intoxication or the final exhaustion of a reserve. The cause of the sudden death is not clearly understood. One of the explanations is that toxic protein degradation products accumulate in the blood because the normal channels of destruction and elimination are not available. It is generally found that carnivorous animals die most rapidly after adrenalectomy.

CORTEX AND BLOOD SUGAR.

In experiments with adrenalectomized rats, Kuriyama (34), Cori and Cori (18), and Artundo (4) noticed a fall in blood sugar. Artundo also found a fall in hepatic and

1. The first part of the document discusses the importance of maintaining accurate records of all transactions and activities. It emphasizes the need for transparency and accountability in financial reporting.

2. The second part of the document outlines the various methods and techniques used to collect and analyze data. It includes a detailed description of the experimental procedures and the statistical analysis performed.

3. The third part of the document presents the results of the study. It includes a series of tables and graphs that illustrate the findings of the research. The data shows a clear trend of increasing activity over time.

4. The fourth part of the document discusses the implications of the findings. It suggests that the results have significant implications for the field of study and may lead to further research in this area.

5. The fifth part of the document provides a conclusion and summarizes the key points of the study. It reiterates the importance of accurate record-keeping and the need for ongoing research in this field.

muscle glycogen.

Wyman and Walker (61) determined the blood sugar of a large number of normal and adrenalectomized rats. Following extirpation of the glands and coincident with the appearance of symptoms of adrenal insufficiency the blood sugar values fell from the normal average of 82 mgs. per cent to about 55 mgs. per cent while in the terminal convulsive stages levels as low as 30 mgs. per cent were reached. They reported that rats which possessed gross accessory cortical tissue, or in which successful cortical transplants had been made, the blood sugar remained within normal limits. From these results they suggested that the cortex is concerned in the steady maintenance of the blood sugar level.

According to one of the prevalent theories the cortex is the primary factor in the maintenance of a normal blood sugar level. Death after adrenalectomy has been attributed by Britton (6) to an abnormal decrease of the blood sugar. He has reported that for some days after operation the blood sugar in cats fluctuated between 70 and 90 mgs. per cent. In cats which showed slight weakness the blood sugar was found to be below the normal range, and in nearly half the cases was below 50 mgs. per cent. Observations on adrenalectomized rats, opossums, squirrels, and ground hogs showed that the blood sugar

TABLE 1*

Blood sugar level in animals (cats) showing symptoms of
adrenal insufficiency.

CAT NUMBER	BLOOD SUGAR	CONDITION	CAT NUMBER	BLOOD SUGAR	CONDITION
	mgm. per cent			mgm. per cent	
252	61	Weak	350	49	Weak
255	67	Weak	357	50	Prostrated
258	43	In Convulsions	359	54	Weak
259	65	In convulsions	360	42	Weak
261	39	In convulsions	363	52	Prostrated
285	39	Weak	365	32	In convulsions
316	57	Very weak	366	41	Weak
316	47	In convulsions	375	25	In convulsions
320		Prostrated	380	52	Weak
323	56	Prostrated	381	59	Weak
338	54	Very weak	383	63	Weak
339	50	Prostrated	386	51	Weak
342	54	Very weak	388	52	Weak
344	51	Prostrated	391	33	In convulsions
346	43	In convulsions	395	32	Very weak

THEORY OF THE EARTH AND ITS HISTORY

CHAPTER I. OF THE ORIGIN OF THE EARTH.

Hypothesis		Hypothesis		Hypothesis	
1	2	3	4	5	6
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979	980	981	982	983	984
985	986	987	988	989	990
991	992	993	994	995	996
997	998	999	1000	1001	1002

values were significantly reduced. He also noticed that corresponding to the decrease of blood sugar there was an increase of blood lactates. The fluctuation of the blood sugar concentration corresponded directly to the degree of adrenal insufficiency. (See Table 1.) Britton, therefore, claims that the cortex of the adrenal glands may be specifically concerned with the storage and utilization of carbohydrates in the body.

CORTICAL EXTRACTS.

The active principle of the adrenal cortex has been obtained with varying success. Stewart and Rogoff (31) claimed to have prepared active extracts of the cortex with lipid solvents. They observed that their extract was not free of adrenalin, but concluded that the results obtained were not due to the presence of adrenalin. They named their cortical extract interrenalin. In adrenalectomized dogs, intravenously injected with interrenalin, the life span was prolonged five or six days over that of control animals. (43)

Hartman and his associates (28) made salt extracts of the adrenal cortex which prolonged the life of cats for twenty-two days or five times the length of an untreated animal. They proposed the name cortin. Hartman used fresh beef adrenals which had been chilled soon after removal from the animal. The extract was not very potent; but it

The first part of the paper discusses the importance of the study of the history of the United States. It is argued that a knowledge of the past is essential for a full understanding of the present. The author then proceeds to discuss the various factors that have shaped the development of the United States, including the role of the government, the influence of the economy, and the impact of the culture.

In the second part of the paper, the author examines the role of the government in the development of the United States. It is argued that the government has played a crucial role in shaping the country's history, from the early years of settlement to the present day. The author then discusses the various ways in which the government has influenced the economy and the culture, and the impact of these influences on the development of the United States.

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contained the active principle of the cortex. Cortin when injected into adrenalectomized rats increases metabolism.

Hartman, Brownell, and Crosby (27) by the use of cortin, have verified the evidence of Wyman and tum Suden (30) that the loss of the adrenal cortex rather than of the medulla is responsible for the lower resistance to cold after adrenal extirpation, and that adrenalectomized rats could be protected against short exposure to cold by autoplasmic cortical transplants. They determined the blood sugar in rats after cooling and found that low temperature and low blood sugar have no definite relation.

Hartman, Brownell, and Lockwood (29) have reported that the administration of cortin diminishes mental fatigue, improves sleep, increases resistance to toxins, increases heat production, brings back normal metabolism, and raises the low blood sugar frequently encountered in the late stage of adrenal insufficiency. They suggest that cortin is a general tissue hormone. If cortin is discontinued in animals with complete adrenal insufficiency or in man with marked insufficiency, it is usually two or three days, sometimes longer, before the symptoms begin to reappear.

Swingle and Pfiffner (53) prepared a cortical extract from beef by the use of alcoholic benzene. The extract is very low in adrenalin content and very effective in combating adrenal insufficiency. This extract may be injected subcutaneously. It is practically free of adrenalin.

The preparation of the Pflüger and Swingle (45) potent extract of beef adrenals may be injected subcutaneously, intraperitoneally, and intravenously. They reported that it can replace complete adrenal cortex insufficiency of animals. Swingle and Pflüger (55) extracts preserved with 0.1 per cent benzoic acid retain their potency for long periods at room temperature; but are thermolabile by boiling for two minutes.

As stated above Britton and Silvette (10) have recently reported that the prepotent function of the adrenal cortex is to regulate the carbohydrate metabolism. They (9) used a modified Swingle and Pflüger (53) extract and further reduced the amount of adrenalin present. Their extract increased the blood sugar when administered intraperitoneally and produced similar changes when from three to five times as much was given orally (8). Reports by these authors indicate that adrenalectomized animals, showing symptoms of the severest insufficiencies, may be brought to normal when cortico-adrenal extracts are injected. After injection, the blood sugar rises gradually and reaches a maximum at the end of the fourth hour. In some cases the rise is to a normal level and in others to 100 mgs. per cent or higher. A gradual decline may be observed at the end of 24 to 48 hours after injection.

They noted that the blood lactates are much increased in the cases of adrenal insufficiency, and that the decrease

The first thing I noticed when I stepped out of the car was the cold, crisp air. It was a relief after the warm, humid weather of the city. I walked towards the entrance of the building, my eyes scanning the architecture. The building was a grand, multi-story structure with a classical facade. The entrance was flanked by two large columns, and a set of stairs led up to a portico. I followed the stairs, my hand resting on the railing. As I reached the top, I saw a group of people standing near a large, ornate chandelier. They were all dressed in formal attire, and I felt a bit out of place. I approached them, and one of the women, a woman with short, dark hair and a friendly smile, greeted me. She introduced me to the others, and we all sat down at a large, round table. The table was set with a white tablecloth, a centerpiece of flowers, and several glasses of water. The food was delicious, and the conversation was lively. I was having a great time, and I was starting to feel like I belonged. The night was young, and the party was just getting started.

of lactates is brought about, along with the increase in blood sugar, by injections of cortico-adrenal extract.

Intraperitoneal injections of the extract into normal cats, rabbits, and rats increased the blood sugar according to Britton and Silvette (9). They observed that the larger the amount of extract injected into operated cats, the greater is the increase in the blood sugar. In general the blood sugar raising power of the extract is a direct function of the amount injected and of the elapsed time after adrenalectomy. (See Table 2.) They found that injections of adrenalin corresponding to the amount present in the extract produced only small increases in blood sugar and that the changes were transitory. The action of glucose solution was only slightly palliative. An intraperitoneal dose of extract represented in cortical tissue from two to three thousand times the amount present in a normal cat. Such a dose lasted from 24 to 48 hours and the hypoglycemic conditions again set in unless re-injections were given. Noxious effects were not observed when such relatively huge amounts of the extract were given intraperitoneally, subcutaneously, intravenously, or intracardially in one or more doses in the course of about twelve hours.

TABLE 2**

Blood sugar changes in adrenalectomized cats following injection of cortico-adrenal extract.

In all cases the animals showed symptoms of insufficiency.

CAT NUMBER	DATE	AMOUNT EXTRACT GIVEN	BLOOD SUGAR			TIME BETWEEN INITIAL And FINAL BLOOD SAMPLES hours
			Before In- jection	After In- jection	In- crease in blood sugar %	
		cc. per kgm.	mgm.	mgm.	%	
255	10/28/30	4	67	94	40	3.0
285	3/3/31	9	39	100	156	18.5
321	2/4/31	8	69	80	16	3.5
323	2/5/31	6	56	68	21	8.0
339	2/16/31	10	50	61	22	4.5
346	2/18/31	10	43	80	86	4.0
350	3/3/31	19	49	135	176	12.0
363	3/2/31	17	41	52	21	12.0
365	3/2/31	8	32	79	147	13.5
366	3/3/31	11	41	147	258	11.0
374	3/9/31	5	34	44	30	1.5
375	3/9/31	5	34	44	30	1.0
375	3/10/31	10	40	100	150	13.0
375	3/12/31	10	27	37	37	5.0
386	3/19/31	30*	65	87	34	24.0
388	3/29/31	10*	52	66	37	18.0
388	4/2/31	20*	57	92	61	2.5
389	4/10/31	20	54	98	66	25.0

Table 1

Summary of the results of the analysis of variance for the effect of the treatment on the response variable.

The analysis of variance was conducted using the following model:

$$Y_{ijk} = \mu + \alpha_i + \beta_j + \gamma_k + \alpha\beta_{ij} + \alpha\gamma_{ik} + \beta\gamma_{jk} + \alpha\beta\gamma_{ijk} + \epsilon_{ijk}$$

Treatment	Response Variable	Mean	Standard Error	t-value	p-value
Control	Yield	1.2	0.1	12.0	0.0001
T1	Yield	1.5	0.1	15.0	0.0001
T2	Yield	1.8	0.1	18.0	0.0001
T3	Yield	2.1	0.1	21.0	0.0001
T4	Yield	2.4	0.1	24.0	0.0001
T5	Yield	2.7	0.1	27.0	0.0001
T6	Yield	3.0	0.1	30.0	0.0001
T7	Yield	3.3	0.1	33.0	0.0001
T8	Yield	3.6	0.1	36.0	0.0001
T9	Yield	3.9	0.1	39.0	0.0001
T10	Yield	4.2	0.1	42.0	0.0001
T11	Yield	4.5	0.1	45.0	0.0001
T12	Yield	4.8	0.1	48.0	0.0001
T13	Yield	5.1	0.1	51.0	0.0001
T14	Yield	5.4	0.1	54.0	0.0001
T15	Yield	5.7	0.1	57.0	0.0001
T16	Yield	6.0	0.1	60.0	0.0001
T17	Yield	6.3	0.1	63.0	0.0001
T18	Yield	6.6	0.1	66.0	0.0001
T19	Yield	6.9	0.1	69.0	0.0001
T20	Yield	7.2	0.1	72.0	0.0001
T21	Yield	7.5	0.1	75.0	0.0001
T22	Yield	7.8	0.1	78.0	0.0001
T23	Yield	8.1	0.1	81.0	0.0001
T24	Yield	8.4	0.1	84.0	0.0001
T25	Yield	8.7	0.1	87.0	0.0001
T26	Yield	9.0	0.1	90.0	0.0001
T27	Yield	9.3	0.1	93.0	0.0001
T28	Yield	9.6	0.1	96.0	0.0001
T29	Yield	9.9	0.1	99.0	0.0001
T30	Yield	10.2	0.1	102.0	0.0001
T31	Yield	10.5	0.1	105.0	0.0001
T32	Yield	10.8	0.1	108.0	0.0001
T33	Yield	11.1	0.1	111.0	0.0001
T34	Yield	11.4	0.1	114.0	0.0001
T35	Yield	11.7	0.1	117.0	0.0001
T36	Yield	12.0	0.1	120.0	0.0001
T37	Yield	12.3	0.1	123.0	0.0001
T38	Yield	12.6	0.1	126.0	0.0001
T39	Yield	12.9	0.1	129.0	0.0001
T40	Yield	13.2	0.1	132.0	0.0001
T41	Yield	13.5	0.1	135.0	0.0001
T42	Yield	13.8	0.1	138.0	0.0001
T43	Yield	14.1	0.1	141.0	0.0001
T44	Yield	14.4	0.1	144.0	0.0001
T45	Yield	14.7	0.1	147.0	0.0001
T46	Yield	15.0	0.1	150.0	0.0001
T47	Yield	15.3	0.1	153.0	0.0001
T48	Yield	15.6	0.1	156.0	0.0001
T49	Yield	15.9	0.1	159.0	0.0001
T50	Yield	16.2	0.1	162.0	0.0001
T51	Yield	16.5	0.1	165.0	0.0001
T52	Yield	16.8	0.1	168.0	0.0001
T53	Yield	17.1	0.1	171.0	0.0001
T54	Yield	17.4	0.1	174.0	0.0001
T55	Yield	17.7	0.1	177.0	0.0001
T56	Yield	18.0	0.1	180.0	0.0001
T57	Yield	18.3	0.1	183.0	0.0001
T58	Yield	18.6	0.1	186.0	0.0001
T59	Yield	18.9	0.1	189.0	0.0001
T60	Yield	19.2	0.1	192.0	0.0001
T61	Yield	19.5	0.1	195.0	0.0001
T62	Yield	19.8	0.1	198.0	0.0001
T63	Yield	20.1	0.1	201.0	0.0001
T64	Yield	20.4	0.1	204.0	0.0001
T65	Yield	20.7	0.1	207.0	0.0001
T66	Yield	21.0	0.1	210.0	0.0001
T67	Yield	21.3	0.1	213.0	0.0001
T68	Yield	21.6	0.1	216.0	0.0001
T69	Yield	21.9	0.1	219.0	0.0001
T70	Yield	22.2	0.1	222.0	0.0001
T71	Yield	22.5	0.1	225.0	0.0001
T72	Yield	22.8	0.1	228.0	0.0001
T73	Yield	23.1	0.1	231.0	0.0001
T74	Yield	23.4	0.1	234.0	0.0001
T75	Yield	23.7	0.1	237.0	0.0001
T76	Yield	24.0	0.1	240.0	0.0001
T77	Yield	24.3	0.1	243.0	0.0001
T78	Yield	24.6	0.1	246.0	0.0001
T79	Yield	24.9	0.1	249.0	0.0001
T80	Yield	25.2	0.1	252.0	0.0001
T81	Yield	25.5	0.1	255.0	0.0001
T82	Yield	25.8	0.1	258.0	0.0001
T83	Yield	26.1	0.1	261.0	0.0001
T84	Yield	26.4	0.1	264.0	0.0001
T85	Yield	26.7	0.1	267.0	0.0001
T86	Yield	27.0	0.1	270.0	0.0001
T87	Yield	27.3	0.1	273.0	0.0001
T88	Yield	27.6	0.1	276.0	0.0001
T89	Yield	27.9	0.1	279.0	0.0001
T90	Yield	28.2	0.1	282.0	0.0001
T91	Yield	28.5	0.1	285.0	0.0001
T92	Yield	28.8	0.1	288.0	0.0001
T93	Yield	29.1	0.1	291.0	0.0001
T94	Yield	29.4	0.1	294.0	0.0001
T95	Yield	29.7	0.1	297.0	0.0001
T96	Yield	30.0	0.1	300.0	0.0001
T97	Yield	30.3	0.1	303.0	0.0001
T98	Yield	30.6	0.1	306.0	0.0001
T99	Yield	30.9	0.1	309.0	0.0001
T100	Yield	31.2	0.1	312.0	0.0001
T101	Yield	31.5	0.1	315.0	0.0001
T102	Yield	31.8	0.1	318.0	0.0001
T103	Yield	32.1	0.1	321.0	0.0001
T104	Yield	32.4	0.1	324.0	0.0001
T105	Yield	32.7	0.1	327.0	0.0001
T106	Yield	33.0	0.1	330.0	0.0001
T107	Yield	33.3	0.1	333.0	0.0001
T108	Yield	33.6	0.1	336.0	0.0001
T109	Yield	33.9	0.1	339.0	0.0001
T110	Yield	34.2	0.1	342.0	0.0001
T111	Yield	34.5	0.1	345.0	0.0001
T112	Yield	34.8	0.1	348.0	0.0001
T113	Yield	35.1	0.1	351.0	0.0001
T114	Yield	35.4	0.1	354.0	0.0001
T115	Yield	35.7	0.1	357.0	0.0001
T116	Yield	36.0	0.1	360.0	0.0001
T117	Yield	36.3	0.1	363.0	0.0001
T118	Yield	36.6	0.1	366.0	0.0001
T119	Yield	36.9	0.1	369.0	0.0001
T120	Yield	37.2	0.1	372.0	0.0001
T121	Yield	37.5	0.1	375.0	0.0001
T122	Yield	37.8	0.1	378.0	0.0001
T123	Yield	38.1	0.1	381.0	0.0001
T124	Yield	38.4	0.1	384.0	0.0001
T125	Yield	38.7	0.1	387.0	0.0001
T126	Yield	39.0	0.1	390.0	0.0001
T127	Yield	39.3	0.1	393.0	0.0001
T128	Yield	39.6	0.1	396.0	0.0001
T129	Yield	39.9	0.1	399.0	0.0001
T130	Yield	40.2	0.1	402.0	0.0001
T131	Yield	40.5	0.1	405.0	0.0001
T132	Yield	40.8	0.1	408.0	0.0001
T133	Yield	41.1	0.1	411.0	0.0001
T134	Yield	41.4	0.1	414.0	0.0001
T135	Yield	41.7	0.1	417.0	0.0001
T136	Yield	42.0	0.1	420.0	0.0001
T137	Yield	42.3	0.1	423.0	0.0001
T138	Yield	42.6	0.1	426.0	0.0001
T139	Yield	42.9	0.1	429.0	0.0001
T140	Yield	43.2	0.1	432.0	0.0001
T141	Yield	43.5	0.1	435.0	0.0001
T142	Yield	43.8	0.1	438.0	0.0001
T143	Yield	44.1	0.1	441.0	0.0001
T144	Yield	44.4	0.1	444.0	0.0001
T145	Yield	44.7	0.1	447.0	0.0001
T146	Yield	45.0	0.1	450.0	0.0001
T147	Yield	45.3	0.1	453.0	0.0001
T148	Yield	45.6	0.1	456.0	0.0001
T149	Yield	45.9	0.1	459.0	0.0001
T150	Yield	46.2	0.1	462.0	0.0001
T151	Yield	46.5	0.1	465.0	0.0001
T152	Yield	46.8	0.1	468.0	0.0001
T153	Yield	47.1	0.1	471.0	0.0001
T154	Yield	47.4	0.1	474.0	0.0001
T155	Yield	47.7	0.1	477.0	0.0001
T156	Yield	48.0	0.1	480.0	0.0001
T157	Yield	48.3	0.1	483.0	0.0001
T158	Yield	48.6	0.1	486.0	0.0001
T159	Yield	48.9	0.1	489.0	0.0001
T160	Yield	49.2	0.1	492.0	0.0001
T161	Yield	49.5	0.1	495.0	0.0001
T162	Yield	49.8	0.1	498.0	0.0001
T163	Yield	50.1	0.1	501.0	0.0001
T164	Yield	50.4	0.1	504.0	0.0001
T165	Yield	50.7	0.1	507.0	0.0001
T166	Yield	51.0	0.1	510.0	0.0001
T167	Yield	51.3	0.1	513.0	0.0001
T168	Yield	51.6	0.1	516.0	0.0001
T169	Yield	51.9	0.1	519.0	0.0001
T170	Yield	52.2	0.1	522.0	0.0001
T171	Yield	52.5	0.1	525.0	0.0001
T172	Yield	52.8	0.1	528.0	0.0001
T173	Yield	53.1	0.1	531.0	0.0001
T174	Yield	53.4	0.1	534.0	0.0001
T175	Yield	53.7	0.1	537.0	0.0001
T176	Yield	54.0	0.1	540.0	0.0001
T177	Yield	54.3	0.1	543.0	0.0001
T178	Yield	54.6	0.1	546.0	0.0001
T179	Yield	54.9	0.1	549.0	0.0001
T180	Yield	55.2	0.1	552.0	0.0001
T181	Yield	55.5	0.1	555.0	0.0001
T182	Yield	55.8	0.1	558.0	0.0001
T183	Yield	56.1	0.1	561.0	0.0001
T184	Yield	56.4	0.1	564.0	0.0001
T185	Yield	56.7	0.1	567.0	0.0001
T186	Yield	57.0	0.1	570.0	0.0001
T187	Yield	57.3	0.1	573.0	0.0001
T188	Yield	57.6	0.1	576.0	0.0001
T189	Yield	57.9	0.1	579.0	0.0001
T190	Yield	58.2	0.1	582.0	0.0001
T191	Yield	58.5	0.1	585.0	0.0001
T192	Yield	58.8	0.1	588.0	0.0001
T193	Yield	59.1	0.1	591.0	0.0001
T194	Yield	59.4	0.1	594.0	0.0001
T195	Yield	59.7	0.1	597.0	0.0001
T196	Yield	60.0	0.1	600.0	0.0001
T197	Yield	60.3	0.1	603.0	0.0001
T198	Yield	60.6	0.1	606.0	0.0001
T199	Yield	60.9	0.1	609.0	0.0001
T200	Yield	61.2	0.1	612.0	0.0001
T201	Yield	61.5	0.1	615.0	0.0001
T202	Yield	61.8	0.1	618.0	0.0001
T203	Yield	62.1	0.1	621.0	0.0001
T204	Yield	62.4	0.1	624.0	0.0001
T205	Yield	62.7	0.1	627.0	0.0001
T206	Yield	63.0	0.1	630.0	0.0001
T207					

TABLE 2**

Blood sugar changes in adrenalectomized cats following injection of cortico-adrenal extract.

In all cases the animals showed symptoms of insufficiency.

CAT NUMBER	DATE	AMOUNT EXTRACT GIVEN	BLOOD SUGAR		In-crease in blood sugar	TIME BETWEEN INITIAL And FINAL BLOOD SAMPLES
			Before in- jection	After in- jection		
		cc. per kgm.	mgm. %	mgm. %	%	hours
398	4/10/31	20	60	84	40	8.5
444	5/18/31	20*	47	159	217	7.0
444	5/25/31	20*	43	147	241	7.5

*Extract given by mouth; all other injections given intraperitoneally.

** Britton, S. W. & H. Silvette Amer. Jour. Physiol. 1931 99
21

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That these cortical preparations have a practical value is established by the facts that they are able not only to prolong indefinitely the life of an adrenalectomized animal, but also to restore it to normal even from the severest symptoms of adrenal insufficiency. Cortin has already proved its value as the specific treatment for the hitherto fatal Addison's disease. The prohibitive cost of cortical extracts and the potential lack of adrenals leaves to the chemists the discovery of the formula of the hormone so that a synthetic product, less expensive and thus more available for the relief of human suffering, may be made.

SUMMARY

1. The anatomy and embryology of the adrenal glands are described.

2. The medulla and cortex though anatomically related are functionally distinct.

3. The active principle of the medulla has to do with rapid adjustments and changes.

4. Adrenalin accelerates the mobilization of blood sugar, the energy fuel par excellence.

5. While adrenalin is not indispensable to life and health, the organism which can muster its energies is most likely to survive. At times of great emergency adrenalin serves normally to integrate the body for strenuous muscular activity.

6. Cannon believes that adrenalin acts primarily on the liver glycogen; but Cori and Cori conclude that the basic action of adrenalin is to accelerate muscle glycogenolysis.

7. About all that is known concerning the function of the adrenal cortex is that it is essential for life.

8. The cortex is concerned with the steady maintenance of certain body conditions either by its ability to control the production or elimination of poisonous waste products or by the maintenance of a normal blood sugar level.

9. Active extracts of the adrenal cortex have been prepared which restore to health totally adrenalectomized animals suffering from severe adrenal insufficiency, and maintain them indefinitely in good condition.

THE HISTORY OF THE
CITY OF BOSTON

FROM THE FIRST SETTLEMENT
TO THE PRESENT TIME
BY
JOHN B. BOWEN
OF THE
CITY OF BOSTON
IN TWO VOLUMES
VOL. I.
BOSTON: PUBLISHED BY
J. B. BOWEN, 1846.

The history of the city of Boston, from the first settlement to the present time, is a subject of great interest and importance. It is a city which has been the seat of many of the most important events in the history of the United States. It has been the birthplace of many of the most distinguished men of the country, and it has been the scene of many of the most important battles and revolutions. The history of the city of Boston is a history of the growth and development of the United States, and it is a history which should be known by every citizen of the country.

The first settlement of the city of Boston was made in 1630, when a group of Puritan settlers, led by John Winthrop, arrived in the city. They were seeking a place where they could practice their religion in freedom, and they found it in Boston. The city grew rapidly, and by 1680 it was one of the largest and most important cities in the colonies. It was the center of the Puritan movement, and it was the seat of many of the most important events in the history of the United States.

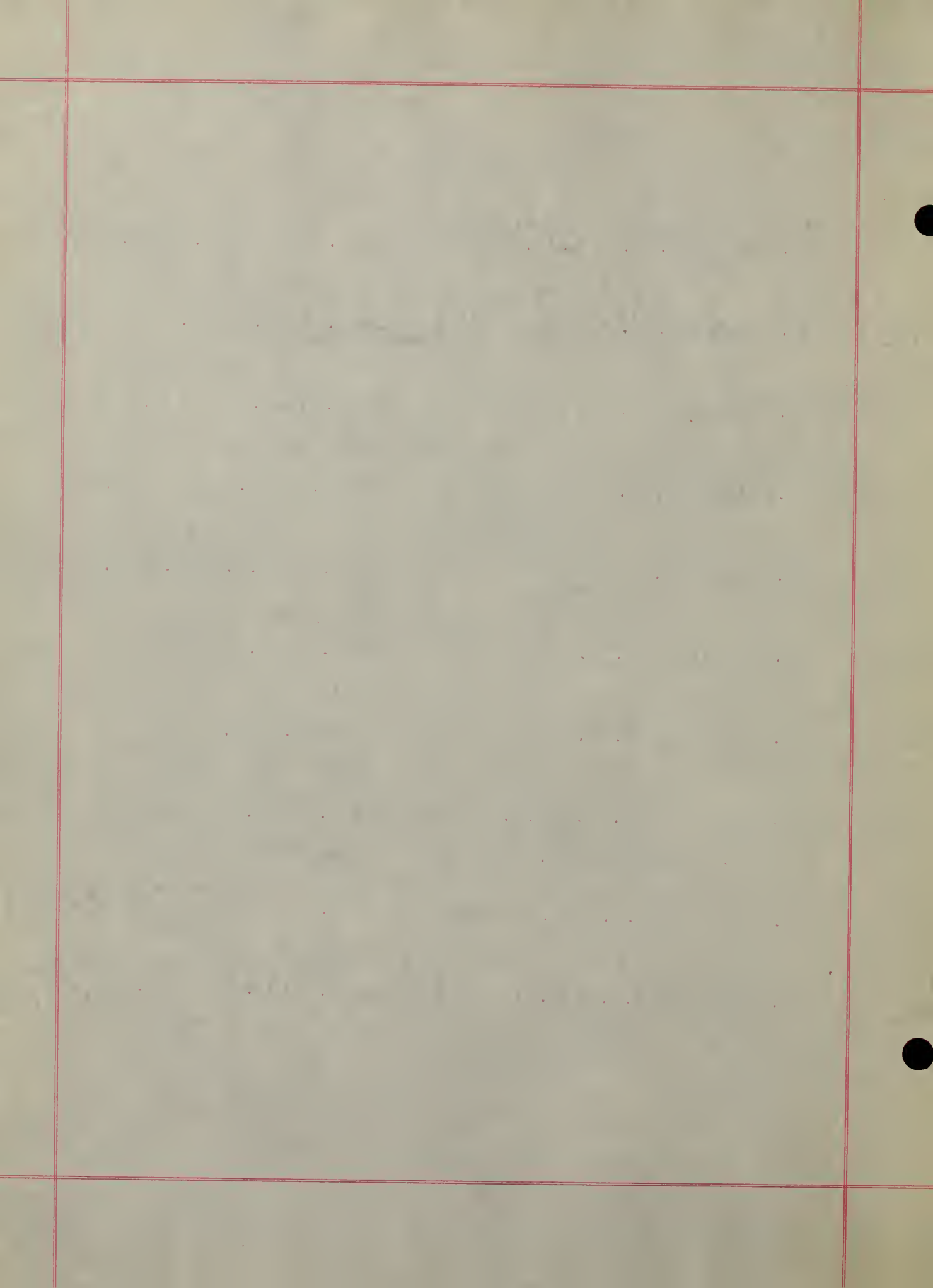
In 1773, the city of Boston was the scene of the Boston Tea Party, a protest against the British tax on tea. This event led to the American Revolution, and it was a turning point in the history of the United States. The city of Boston was the birthplace of the American Revolution, and it was the seat of many of the most important events in the history of the United States.

The city of Boston has been the seat of many of the most important events in the history of the United States. It has been the birthplace of many of the most distinguished men of the country, and it has been the scene of many of the most important battles and revolutions. The history of the city of Boston is a history of the growth and development of the United States, and it is a history which should be known by every citizen of the country.

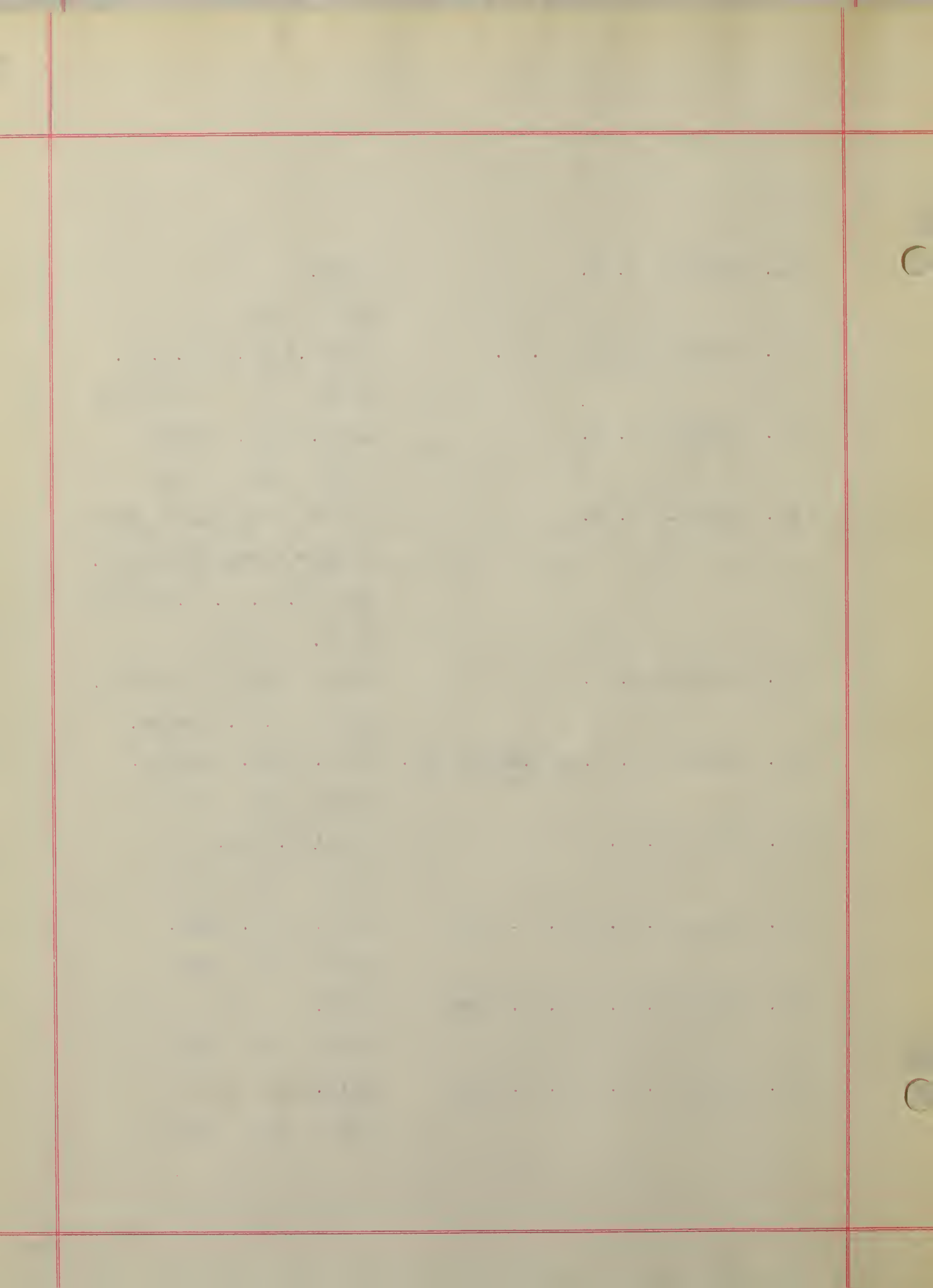
10. These extracts restore and maintain animals at a normal blood sugar level.

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1. The first part of the paper is devoted to the study of the

properties of the function $f(x)$ defined by the equation

$$f(x) = \int_0^x \frac{1}{1+t^2} dt$$

and to the study of the function $F(x)$ defined by the equation

$$F(x) = \int_0^x f(t) dt$$

and to the study of the function $G(x)$ defined by the equation

$$G(x) = \int_0^x F(t) dt$$

and to the study of the function $H(x)$ defined by the equation

$$H(x) = \int_0^x G(t) dt$$

and to the study of the function $I(x)$ defined by the equation

$$I(x) = \int_0^x H(t) dt$$

and to the study of the function $J(x)$ defined by the equation

$$J(x) = \int_0^x I(t) dt$$

and to the study of the function $K(x)$ defined by the equation

$$K(x) = \int_0^x J(t) dt$$

and to the study of the function $L(x)$ defined by the equation

$$L(x) = \int_0^x K(t) dt$$

and to the study of the function $M(x)$ defined by the equation

$$M(x) = \int_0^x L(t) dt$$

and to the study of the function $N(x)$ defined by the equation

$$N(x) = \int_0^x M(t) dt$$

and to the study of the function $O(x)$ defined by the equation

$$O(x) = \int_0^x N(t) dt$$

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